Regulatory Directive DIR2008-01

Registering a New Source of Technical Grade Active Ingredient Under the Protection of Proprietary Interests in Pesticide Data Policy

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1.0 Introduction

Regulatory Directive DIR2007-03, *Protection of Proprietary Interests in Pesticide Data* (PPIP) describes a new data protection policy that replaces the Product-Specific Registration policy (PSR II) published in Trade Memorandum T-1-249, *Product-Specific Registration and Proprietary Rights to Data*, on 8 July 1987. Under this new policy, data from technical grade active ingredient (TGAI), manufacturing concentrate and end-use product that meet certain criteria are protected. As the policy will be phased in starting with TGAIs, this document provides guidance on how to apply under the PPIP policy for registration of a new source of a registered TGAI based on an existing database. The document also describes procedures and timelines that Health Canada's Pest Management Regulatory Agency (PMRA) intends to follow. This approach will be reassessed in the upcoming months based on the experience gained and on the comments received. The PMRA will also publish guidelines for the registration of generic manufacturing concentrates and end-use products in the near future.

For new sources of TGAI, the policy does not apply in the following cases.

- The applicant is relying on his own database or on publicly available studies.
- The applicant has previously gained access to a relevant database through PPIP or the former PSR II policy and has provided evidence of this, i.e. a letter of access for PPIP and the application number for PSR II.

As stated in DIR2007-03, there are three types of database protection status: exclusive, compensable and generic. Applications to register a new source of TGAI where the registered TGAI database has an exclusive protection status can only proceed if the applicant has provided a letter of access to the protected database or if the applicant has provided a full database. In the absence of a letter of access, the Agency will only consider requests to establish equivalency between the proposed and registered TGAIs if the exclusive protection has less than one remaining year.

This guidance document has three sections. The first section describes the application process to register a new source of TGAI. This first section is further subdivided into two subsections, one providing information to the applicants[1] and the other to the registrants[2] of the cited products. The second section describes the overall process, while the third section describes the process for adding a major new use that was previously added to another source of an equivalent TGAI.

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1 An applicant is someone seeking registration of a pest control product.

2 A registrant is an owner of a registered pest control product.

2.0 Registration of a New Source of Technical Grade Active Ingredient Based on an Existing Database

2.1 Information to Applicants

An application to register a new source of TGAI based on an existing database will require the following.

- Cover letter
- Application form
- Fee Form and appropriate fees
- Statement of Product Specification Form (SPSF)
- Chemistry data (Part 2) for conventional chemical or Product Characterization and Analysis (Part M2) for Microbial pest control products
- Text label
- e-index in XML format
- Copy of a letter informing current registrant(s) of the active ingredient of the applicant's intention to register a new source of this active ingredient

2.1.1 Cover Letter

The letter must state that the purpose of the application is to register a new source of TGAI and that the applicant wishes to rely on an existing database through the PPIP policy. If the applicant is already a member of a task force, it should be stated in the application letter and be accompanied by a letter from the task force confirming that the applicant has access to their data.

2.1.2 Application Form

The application form must indicate Category B—Other

2.1.3 Fees

For an application relying on a previously submitted database, the fees will be limited to Part 1B (Label) and Part 2 (Chemistry). The full fees should be submitted initially to avoid having the application put on hold at the end of the screening step.

2.1.4 Product Specification Form and Chemistry Data

All new sources of TGAI are required to submit an SPSF and a complete Part 2 chemistry data package (or Part M2 for Microbials) in order to establish equivalency to the registered source(s). The data requirements for a new source of TGAI are identified in Appendix I. Additional data may be required should issues of concern be identified (e.g. presence of certain microcontaminants).

2.1.5 Label

The label of the proposed TGAI should conform to the label of the most recent registered source of TGAI. If the active ingredient was re-evaluated, the label should include, where applicable, any changes requested. Labels and re-evaluation decision documents can be found on the PMRA's website.

2.1.6 E-index

The e-index is an electronic index in XML format that describes each document submitted. Please refer to Regulatory Directive DIR2006-05, *Requirements for Submitting Data Index, Documents and Forms*.

2.1.7 Letter to Current Registrants

As the PPIP policy is based on time-limited negotiation, the current registrants must be informed early in the process of the upcoming negotiation. This will allow the registrants to initiate the process of identifying their protected data and will allow both parties to prepare for the upcoming negotiation. The Agency is therefore requiring that the applicant contact all current registrants of the TGAI at the same time that they apply to register a new source of TGAI. All registrants must be contacted as the applicant must gain access to a complete set of protected data, whether it is from a single registrant or from a combination of registrants. A list of the current registrants and their addresses can be obtained from the PMRA. The letter should be based on the template found in Appendix II.

2.2 Information to Registrants

Request for Identification of Protected Data

The PMRA requires that applicants contact all the registrant(s) of the currently registered source(s) to inform them of their intention to register a new source of a TGAI based on the existing database. The PMRA will also contact the registrant(s) during the review process to request the list of protected data[3]. However, the PMRA will require that the list of protected data be provided within 30 days, and the negotiation will be time limited. Consequently, the registrants should start to identify their protected data and discuss with the applicant the upcoming negotiation process upon receipt of the applicant's letter. It should be noted that the Agency will proceed as if the database was generic should the registrant fail to provide the list of protected data in time. In such a case, the applicant would not have to compensate the registrant for any protected data. In cases where there are multiple registrants, the applicant may not have to negotiate with all of them as long as the applicant can gain access to a database covering all protected data.

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3 Registrants of products under the exclusive protection status do not need to prepare a list of protected studies. The PMRA will inform the applicant of this status.

The list of protected data must be in the form presented in Appendix III. The eligibility criteria are presented in DIR2007-03. It should be noted that only the registrant will be contacted as the PMRA is usually not aware of business contracts with other data owners. Therefore, the registrant will be responsible for identifying all protected data that was submitted to the PMRA in support of their source of TGAI, including data provided by a third party[4]. Outstanding data requirements from conditional registration, from the re-evaluation process or a special review may be identified separately as applicants may want to come to an agreement on those as well. However, applicants do not have to negotiate an agreement on data that has not been submitted at the time of the request, but will have to commit to provide the outstanding data by a specified time.

3.0 Overall Process

3.1 Verification

Upon receipt of an application to register a new source of active ingredient through the PPIP policy, the Agency will send, within seven days, an acknowledgement to the applicant indicating that the submission was received.

3.2 Screening

This is a 45-day step where the information provided is verified for completeness and thoroughly screened. Should there be significant information or studies missing, or if the fees have not been paid in full before going to the review process, the application will be put on hold for 45 days to allow for submission of the fees or the missing information. If there is no response or if the response is incomplete or inadequate, the application is withdrawn and returned to the applicant at the applicant's expense.

The Agency will also verify if the registered TGAI is under exclusive protection. If the database is no longer under exclusive protection, the Agency will send a letter to the registrant to request that a list of protected data be submitted within 30 days. If the database is still under exclusive protection, the submission will only proceed to establish chemical equivalency if a letter of access to an existing database was submitted or if there is less than one year remaining in the exclusive protection period. In these cases, a letter would also be sent to the current registrant to inform them that a list of protected studies does not need to be generated.

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4 The PMRA has agreed in the past to specific data protection provisions for certain task force data. These agreement will be maintained until the protection lapses.

3.3 Review/Evaluation

Following completion of the screening step, the part 2 chemistry data (or M2 for microbials) will be reviewed for chemical equivalency (biological equivalency for microbials) to a currently registered source. The PMRA intends to establish whether a new source of TGAI is equivalent to the registered source within 60 days for conventional chemicals and 120 days for microbial products. Should data gaps be identified, the application will be put on hold for 90 days to allow submission of the missing information. If the requested data are submitted, they are screened within 45 days and the full time for completing the review is applied. Lack of, or an inadequate response within 90 days results in the application being withdrawn and returned to the applicant at the applicant's expense.

The equivalence between two sources of conventional chemical will be based on criteria identified in Appendix IV. The Agency recognizes that some new sources of active ingredients not meeting these criteria may actually represent a reduced risk to human health or to the environment. For example, a product may have a guarantee above the specified threshold but may also have reduced level of contaminants. Consequently, TGAIs that do not meet these criteria may still qualify for registration. However, TGAIs not meeting the equivalency criteria will require further science review (e.g. toxicology) to assess the significance of the differences. This will result in a longer review time of up to an additional 90 days.

Should it be determined that the applicant's product is not equivalent to a registered source and that the differences with the registered sources are not acceptable, the submission will be withdrawn. The applicant will have to re-apply as a Category A, new active ingredient, and submit a full package in order to register their product.

3.4 Protected Data Identification

Concurrent with the equivalency assessment, the PMRA will verify within 30 days the list of protected data received from the current registrants. Should there be studies not meeting the criteria outlined in DIR2007-03, the PMRA will provide a revised list to the registrant who will then have 15 days to appeal and provide proof that the data identified meets the protection criteria. The PMRA will review the information provided and make a final decision. Should there be no protected data or should the registrant fail to provide a list of protected studies in time, the database will be considered generic and the submission will proceed to label review following establishment of equivalency.

3.5 Negotiation/Binding Arbitration

Once equivalency has been established between the sources of TGAI and the list of protected data has been confirmed, both the applicant and the registrant will receive a letter from the PMRA requesting that the negotiation process start. Applicant and registrant(s) will have 120 days to complete negotiations. This time line may be extended at the request of both parties. However, the submission may be withdrawn should the negotiation period be extended by more than 60 days and the applicant would have to reapply for registration. The PMRA will not get involved in the negotiation process, but may provide clarification on the data list provided.

Upon completion of the negotiation the registrant will have to submit a letter based on the template found in Appendix V to allow the applicant to rely on their database. The PMRA will consider that the applicant can rely on all data identified in the list initially provided by the PMRA. As mentioned in DIR2007-03, the involved parties may negotiate access to only a subset of the data, but the PMRA will not enforce a business agreement on behalf of the companies. For example, applicants could negotiate access to data covering only some of the registered uses, but the PMRA would consider that they have access to the whole currently registered use pattern.

In cases where an agreement could not be obtained during the 120-day mandatory negotiation, either party can request binding arbitration. The applicant will then have to send a letter to the PMRA and the other companies involved indicating that the matter will be brought to binding arbitration. The PMRA will not get involved in the arbitration process. In order to continue with the registration process, the applicant will then have to send a letter to the registrant(s) and the PMRA indicating that they commit to comply with the arbitration decision. In the absence of such commitment, the PMRA will withdraw the submission after the 120-day negotiation period. The arbitration procedure will have to be concluded and a letter of access from the registrant(s) provided to PMRA within a year of registration.

3.6 Label

The proposed label will be reviewed during the equivalency assessment. Any required changes will be sent to the applicant after the equivalency has been established. The applicant will then have 45 days to revise and translate the label. Upon receipt, the PMRA will verify that the required amendments have been made and that the translation is accurate.

3.7 Registration

After receiving the letter of access from the registrant(s) or a commitment from the applicant to proceed with binding arbitration and comply with the arbitration decision, the Agency will check within 30 days whether there are any outstanding data requirements (e.g. from conditional registration). Should that be the case, the applicant will be asked to commit within 30 days to provide the data or gain access to it within a specified time frame. Once the letter of access from the registrant (or applicant's commitment to follow arbitration decision), the final labels and the letter of commitment for the outstanding data (if applicable) have been received, the Agency will proceed with the registration of the new source of TGAI.

4.0 Adding New Use Sites to a Currently Registered Source of Technical Grade Active Ingredient Based on an Existing Database

TGAIs have defined use patterns referred to as use-site categories (USCs). This means that a TGAI can only be used to manufacture an end-use pest control product for a use pattern that matches the TGAI's USC. Additional USCs can be added to a TGAI after their first registration and this usually requires the submission of additional data under a Category A. However, only the registrant who provided the additional data obtains the additional USC for their TGAI.

In order to add an existing USC to their own source of TGAI, registrants must:

- provide their own data;
- provide a letter of access to an existing database covering the new use pattern; or
- gain access to an existing database covering the new use pattern through PPIP.

The process to gain access to an existing database is similar to the one followed for the registration of a new source of technical grade active ingredient with the following modifications.

- The application letter will have to identify the data to which the applicant already has access and provide the letter of access from the owner of the data.
- The existing chemistry data will be assessed during initial review, and if gaps are identified or equivalency to the cited TGAI is no longer valid (e.g. reduction in microcontaminant levels), new data will be requested.
- Only the registrant(s) of the TGAI with the additional use pattern will need to be contacted.
- Fees will only be required for the label unless other data were required following the initial review.

Appendix I Chemistry Data Requirement for a New Source of Technical Grade Active Ingredients

Data Code	Title	Data Required	Conditions	Volume Number and Pages
0	**Index**	R		
1	**Label**	R		
2	**Chemistry requirements for the registration of a technical grade of active ingredient or an integrated system product**			
2.1	Applicant's name and office address	R		
2.2	Manufacturer's name and office address and manufacturing plant's name and address	R		
2.3	Product trade name	R		
2.3.1	Other names	R		
2.4	Common name	R		
2.5	Chemical name	R		
2.6	Chemical Abstracts Registry Number	R		
2.7	Structural formula	R		
2.8	Molecular formula	R		
2.9	Molecular weight	R		
2.11	**Manufacturing Methods for the TGAI**			
2.11.1	Manufacturing Summary	R		
2.11.2	Description of starting materials	R		
2.11.3	Detailed production process description	R		
2.11.4	Discussion of formation of impurities	R		
2.12	**Specifications**			
2.12.1	Establishing certified limits	R		
2.12.2	Control product specification form	R		
2.13	**Preliminary Analysis**			
2.13.1	Methodology/Validation	R		
2.13.2	Confirmation of identity	R		
2.13.3	Batch data	R		
2.13.4	Impurities of toxicological concern	CR	If applicable	
2.14	**Chemical and Physical Properties**			
2.14.1	Colour	R		

Data Code	Title	Data Required	Conditions	Volume Number and Pages
2.14.2	Physical state	R		
2.14.3	Odour	R		
2.14.4	Melting point / melting range	R	Solid at room temperature	
2.14.5	Boiling point / boiling range	R	Liquid at room temperature	
2.14.6	Density or specific gravity	R	See 8.2.1	
2.14.7	Water solubility (mg/L)	R	See 8.2.1	
2.14.8	Solvent solubility (mg/L)	R		
2.14.9	Vapour pressure	R	See 8.2.1	
2.14.10	Dissociation constant	R	See 8.2.1	
2.14.11	Octanol-water partition coefficient	R	See 8.2.1	
2.14.12	UV/Visible absorption spectra	R	See 8.2.1	
2.14.13	Stability (temperature, metals)	R		
2.14.14	Storage stability data	R		
2.15	Sample(s) of analytical standards and ROC	R		
2.16	Other studies/data/reports	CR	If available	

Appendix II Template Letter From Applicant to the Current Registrant(s)

[COMPANY LETTERHEAD]

Date

Name of Registrant
Address of Registrant

Dear :

Re: [Name of product and Registration No.]

Please be advised that [NAME OF APPLICANT] has submitted to Health Canada's Pest Management Regulatory Agency (PMRA) an application to register a new source of the active ingredient [NAME OF ACTIVE INGREDIENT]. According to Regulatory Directive 2007-03, *Protection of Proprietary Interests in Pesticide Data in Canada,* [NAME OF APPLICANT] has to gain access through mandatory negotiation and possibly through binding arbitration to a complete set of protected data. These data can be from a single registrant who owns a copy of all protected studies or by a combination of registrants each having a subset of the protected data. In order to proceed, all registrants of [NAME OF ACTIVE INGREDIENT] will have to provide to the PMRA a list of their protected data. Therefore, [NAME OF REGISTRANT] should expect to be contacted shortly by the PMRA with a request to submit within 30 days a list of your protected data. Please prepare accordingly.

The purpose of this letter is also to inform you that you will be contacted shortly to initiate discussion about the upcoming negotiation process.

Thank you for your cooperation in this matter.

[Applicant's signature]
[Printed signatory name and contact information]

Appendix III Template for the Index of Protected Data

PMRA Number[1]	Registrant	Application No. OR Re-evaluation Reference No.[2]	Pest Control Product Registration No.	DACO	DACO Description	Title of Study[3]	Active Ingredient or Other Test Compound	Application Date[4]
987654	ABC Inc.	2001-9999	12345	4.6.1	Acute Oral		Dihydrogen oxide	15 Jan 2013
N/A	ABC Inc.	2002-9999 USEPA RED	12345	9.5.2.1	Acute Cold Water Fish (rainbow trout)		Dihydrogen oxide	19 Mar 2011
123654	Task force XYZ	2003-9999	12345	4.5.14	Develop-mental Neuro-toxicity		Dihydrogen oxide	6 Jun 2015

1 If known.

2 For the United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) data, the PMRA re-evaluation reference number should also be quoted.

3 Required in cases where the study title differs from the data code (DACO) title.

4 Date of the application under which the data were submitted to the PMRA or Program 1 initiation date for USEPA RED data.

Appendix IV Criteria for Chemical Equivalency of TGAI

- The active ingredient must be identical.
- The manufacturing process should be similar.
- The guarantee of the active ingredient in the new TGAI must be ± 5% relative to the guarantee in the cited TGAI (e.g. for a registered TGAI having a guarantee of 80%, the acceptable guarantee range for the proposed TGAI would be 76% to 84%).
- The total weight of non-identical impurities must be below 5%.
- The microcontaminant levels must be equal to or lower than in the currently registered source.
- The chemistry data (part 2) must be complete.

NOTE: A TGAI not meeting the above criteria may still qualify for registration and the differences will be assessed on a case-by-case basis.